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Heritable influences on amygdala and orbitofrontal cortex contribute to genetic variation in core dimensions of personality

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ABSTRACT

While many studies have reported that individual differences in personality traits are genetically influenced, the neurobiological bases mediating these influences have not yet been well characterized. To advance understanding concerning the pathway from genetic variation to personality, here we examined whether measures of heritable variation in neuroanatomical size in candidate regions (amygdala and medial orbitofrontal cortex) were associated with heritable effects on personality. A sample of 486 middle-aged (mean = 55 years) male twins (complete MZ pairs = 120; complete DZ pairs = 84) underwent structural brain scans and also completed measures of two core domains of personality: positive and negative emotionality. After adjusting for estimated intracranial volume, significant phenotypic (r_p) and genetic (r_g) correlations were observed between left amygdala volume and positive emotionality ($r_p = .16$, $p < .01$; $r_g = .23$, $p < .05$, respectively). In addition, after adjusting for mean cortical thickness, genetic and nonshared-environmental correlations (r_e) between left medial orbitofrontal cortex thickness and negative emotionality were also observed ($r_g = .34$, $p < .01$; $r_e = -.19$, $p < .05$, respectively). These findings support a model positing that heritable bases of personality are, at least in part, mediated through individual differences in the size of brain structures, although further work is still required to confirm this causal interpretation.

Introduction

Delineating the etiology of individual differences in personality constitutes a fundamental challenge in the human behavioral sciences. Considerable work in recent decades has demonstrated that genetic influences underpin individual differences in personality (Jang et al., 1996; Loehlin et al., 1998; Riemann et al., 1997; Tellegen et al., 1988); however, comparatively little work has identified the neurobiological substrates mediating these genetic influences (DeYoung and Gray, 2009). Whereas standard approaches to localizing neural correlates of personality typically employ functional imaging methods (Canli et al., 2002), recent work has illustrated that regional gray matter volume is also related to variation in such traits (DeYoung et al., 2010; Kanai and Rees, 2011; Lewis et al., 2012, 2013). However, although examinations of regional gray matter correlates have been combined with genetically-informative designs in prior work examining traits such as cognitive ability (Posthuma et al., 2002), to the best of our knowledge, no study has yet examined whether individual differences in regional brain size share common heritable variation with personality traits. Evidence that these levels of analysis share a common genetic basis would help to significantly advance biological understandings of personality. Accordingly, the current study examined whether two major dimensions of personality – positive emotionality and negative emotionality – were linked to genetic influences on individual differences in regional brain size.

Biological bases of personality: from behavioral genetics to neuroanatomy

Understanding the origins of personality has been an enduring and major endeavor for human behavioral research (Eysenck, 1967; Gray

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and McNaughton, 2000; McCrae and Costa, 1999; Tellegen, 1985; Zuckerman, 2005). Behavioral genetic methods, including the twin and family designs, have facilitated such research agendas, allowing individual differences in personality to be decomposed into genetic and environmental components, with work in this area robustly showing genetic influences on personality. For instance, approximately 40%–60% of the variance in 11 primary and 3 higher-order factors on Tellegen's Multidimensional Personality Questionnaire was attributable to genetic influences (Tellegen et al., 1988). Twin analyses examining the Five-Factor Model (FFM) traits reported that individual differences were approximately 50% heritable for all of the FFM traits in adulthood (Jang et al., 1996). This finding is consistent for earlier measures of personality such as Eysenck's Neuroticism and Extraversion scales (Eaves et al., 1998; Floderus-Myrhed et al., 1980), and it has been replicated in several other studies (Loehlin et al., 1998; Riemann et al., 1997), across multiple cultural groupings (Yamagata et al., 2006).

Such work supports a model positing that variation in personality is reflective of individual differences in neurobiology (DeYoung et al., 2010; McCrae and Costa, 1999), especially given the well-established genetic influences on brain measures from twin, and more recently genetic association, studies (Blokland et al., 2012; Kremen et al., 2010a; Schmitt et al., 2007; Toga and Thompson, 2005; Thompson et al., 2014). Although neurobiological models of personality have a long history (Eysenck, 1967), only recently has regional variation in the cortical and subcortical gray matter been associated with variation in personality traits (DeYoung et al., 2010; Kanai and Rees, 2011), with most of this work focusing on the two most central dimensions of personality (Eysenck and Eysenck, 1969; McCrae and Costa, 1999; Tellegen and Waller, 2008): the tendency to express positive affect and proactively engage in the world (extraversion/positive emotionality), and the tendency to express negative affect and to break down under stress (neuroticism/negative emotionality).

In the current study, we also examined these two core dimensions, operationalized here by positive emotionality and negative emotionality, two of the major personality dimensions in the Multidimensional Personality Questionnaire (Tellegen et al., 1988; Tellegen, 1985). These constructs are not isomorphic with extraversion and neuroticism as operationalized in the Big Five or Five-Factor Model of personality (John et al., 2008), but the respective constructs do share important features and are highly correlated (Church, 1994; Clark and Watson, 1999; Klein et al., 2011; Tellegen and Waller, 2008). Research on these two traits has high theoretical importance both to basic personality theory — they are included in most personality lexicons (Eysenck and Eysenck, 1969; McCrae and Costa, 1999; Tellegen and Waller, 2008), as well as because of the translational value that will likely follow a deeper understanding of the underlying biology of these psychiatrically-relevant traits. Indeed, there are robust links between positive and negative emotionality and a range of mood disorders including major depression (Fanous et al., 2007), generalized anxiety disorder (Bienvenu and Stein, 2003), and various personality disorders (Krueger et al., 2012; Saulsman and Page, 2004; Samuel and Widiger, 2008).

Of the studies to address gray matter correlates of positive emotionality/extraversion, specific brain regions are noteworthy as having shown replicable links in independent samples. In particular, medial orbitofrontal cortex (mOFC) has been reported to be larger in individuals with higher scores of extraversion (Cremers et al., 2011; DeYoung et al., 2010; Rauch et al., 2005), with amygdala also showing positive links to extraversion (Cremers et al., 2011; Omura et al., 2005). Broadly similar associations have been reported for neuroticism/negative emotionality, although here *smaller* amygdala and mOFC volumes have been found to associate with higher scores on such constructs. For instance, individuals with panic disorder, which in turn shows strong links to neuroticism (Kotov et al., 2010), were noted, on average, to have smaller amygdala volumes (Hayano et al., 2009). Similarly, higher neuroticism in a sample of healthy adults has been related to smaller amygdala volume (Omura et al., 2005). Research has also shown a negative association between neuroticism and OFC volume (Jackson et al., 2011; Wright et al., 2006). This work has been complemented by recent research (Fuentes et al., 2012), which reported that scores on the behavioral inhibition system scale (Carver and White, 1994) – a construct with strong links to neuroticism (Smits and Boeck, 2006) – were inversely associated with mOFC volume.

While numerous other regions have shown links to personality (DeYoung et al., 2010), the associations with amygdala and OFC appear to be the most robust findings to date. These associations also seem to cohere with recent work on the function of these brain regions. Indeed, amygdala and orbitofrontal cortex function and their interplay are both linked with sensitivity to reward (Gottfried et al., 2003) – a close analogue of extraversion (Depue and Collins, 1999), and sensitivity to threat and fearfulness (Dolan and Vuilleumier, 2003) – which closely describes trait neuroticism (Eysenck, 1967).

The current study

Research demonstrating links between regional brain structure and personality supports the possibility that the pathway from genetic variation to individual differences in personality may be mediated via variation in regional brain structure. To date, however, no work has addressed this possibility. The importance of addressing whether brain structure plays a role in the pathway from genes to personality is of particular salience given that both personality traits (Jang et al., 1996; Tellegen et al., 1988) and regional brain size (Kremen et al., 2010a; Thompson et al., 2014; Toga and Thompson, 2005) have moderate to high heritabilities. To advance understanding on the pathway linking genetic variation and personality, we examined whether size differences in amygdala and mOFC (see Fig. 1) were genetically linked to positive emotionality and negative emotionality. While additional brain regions may be associated with personality, we restricted our

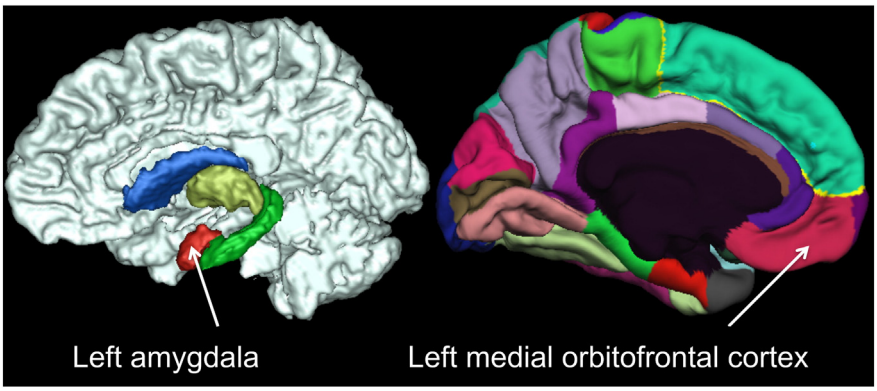

Fig. 1. Anatomical location of left amygdala based on subcortical segmentation and left medial orbital frontal cortex based on cortical parcellation in Freesurfer.